

SUBSTITUTE FORM PTO-1449 U.S. DEPARTMENT OF COMMERCE (MODIFIED) PATENT AND TRADEMARK OFFICE INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use several sheets if necessary) (37 C.F.R. § 1.98(b))	Attorney Docket No.	50125/102001
	Serial No.	10/540,958
	Applicant	Stürzebecher et al.
	Filing Date	January 3, 2006
	Group	1612
	IDS Filed	April 8, 2010

U.S. PATENT DOCUMENTS			
Examiner's Initials	Document Number	Publication Date	Patentee or Applicant
	5,518,735	May 21, 1996	Stürzebecher et al.
	5,602,253	Feb. 11, 1997	Antonsson et al.
	5,705,487	Jan. 06, 1998	Schacht et al.
	5,707,966	Jan. 13, 1998	Schacht et al.
	5,710,130	Jan. 20, 1998	Schacht et al.
	5,726,159	Mar. 10, 1998	Schacht et al.
	5,863,929	Jan. 26, 1999	Klimkowski et al.
	5,914,319	Jun. 22, 1999	Schacht et al.
	6,030,972	Feb. 29, 2000	Böhm et al.
	6,472,393	Oct. 29, 2002	Aliagas-Martin et al.
	6,586,405	Jul. 01, 2003	Semple et al.
	6,624,169	Sep. 23, 2003	Wilhelm et al.
	6,831,196	Dec. 14, 2004	Stürzebecher et al.
	6,841,702	Jan. 11, 2005	Magdolen et al.
	7,038,074	May 2, 2006	Moroder et al.
	7,049,460	May 23, 2006	Magdolen et al.
	7,208,521	Apr. 24, 2007	Magdolen et al.
	7,407,982	Aug. 5, 2009	Steinmetzer et al.
	7,538,216	May 26, 2009	Sperl
	7,608,623	Oct. 27, 2009	Sperl et al.

EXAMINER <u>/Marcos Sznaidman/</u>	DATE CONSIDERED <u>12/02/2010</u>
EXAMINER: Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with the next communication to applicant.	

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.S./

SUBSTITUTE FORM PTO-1449 (MODIFIED) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use several sheets if necessary) (37 C.F.R. § 1.98(b))	Attorney Docket No.	50125/102001
	Serial No.	10/540,958
	Applicant	Stürzebecher et al.
	Filing Date	January 3, 2006
	Group	1612
	IDS Filed	April 8, 2010

U.S. PATENT DOCUMENTS			
	2004/0266766	Dec. 30, 2004	Sperl
	2005/0119190	Jun. 2, 2005	Stürzebecher et al.
	2005/0176993	Aug. 11, 2005	Stürzebecher et al.
	2006/0068457	Mar. 30, 2006	Ziegler et al.
	2007/0055065	Mar. 8, 2007	Stürzebecher et al.
	2007/0066539	Mar. 22, 2007	Stürzebecher et al.
	2008/0261998	Oct. 23, 2008	Sperl et al.
	2009/0117185	May 7, 2009	Steinmetzer et al.
	2010/0022781	Jan. 28, 2010	Steinmetzer et al.

FOREIGN PATENT OR PUBLISHED FOREIGN PATENT APPLICATION				
Examiner's Initials	Document Number	Publication Date	Country or Patent Office	Translation (Yes/No)
	CA 2412181	Dec. 9, 2002	Canada	
	CH 689 611	Jul. 15, 1999	Switzerland	Abstract
	DE 100 29 014	Dec. 20, 2001	Germany	Abstract
	DE 100 29 015	Dec. 20, 2001	Germany	
	DE 102 10 590	Mar. 11, 2002	Germany	
	DE 102 12 555	Sep. 25, 2003	Germany	Abstract
	DE 103 01 300	Jul. 29, 2004	Germany	Abstract
	DE 42 43 858	Jun. 30, 1994	Germany	Abstract
	EP 0 183 271	Jun. 04, 1986	EPO	

EXAMINER	/Marcos Sznajdman/	DATE CONSIDERED	12/02/2010
EXAMINER: Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with the next communication to applicant.			

~~ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.S./~~

SUBSTITUTE FORM PTO-1449 (MODIFIED)	U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	Attorney Docket No.	50125/102001
		Serial No.	10/540,958
		Applicant	Stürzebecher et al.
		Filing Date	January 3, 2006
		Group	1612
		IDS Filed	April 8, 2010
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use several sheets if necessary)			
(37 C.F.R. § 1.98(b))			

FOREIGN PATENT OR PUBLISHED FOREIGN PATENT APPLICATION				
	EP 0 669 317	Aug. 30, 1995	EPO	
	EP 0 672 658	Sep. 20, 1995	EPO	
	EP 1 364 960	Nov. 26, 2003	EPO	
	WO 92/08709	May 29, 1992	WIPO	Abstract
	WO 94/18185	Aug. 18, 1994	WIPO	Abstract
	WO 94/29336	Dec. 22, 1994	WIPO	
	WO 95/17885	Jul. 06, 1995	WIPO	
	WO 95/29189	Nov. 02, 1995	WIPO	
	WO 96/25426	Aug. 22, 1996	WIPO	Abstract
	WO 97/23499	Jul. 3, 1997	WIPO	
	WO 99/05096	Feb. 4, 1999	WIPO	
	WO 00/04954	Feb. 3, 2000	WIPO	Abstract
	WO 00/05245	Feb. 3, 2000	WIPO	
	WO 00/14110	Mar. 16, 2000	WIPO	
	WO 00/17158	Mar. 30, 2000	WIPO	Abstract
	WO 00/58346	Oct. 5, 2000	WIPO	
	WO 00/64470	Nov. 2, 2000	WIPO	
	WO 01/81314	Nov. 1, 2001	WIPO	
	WO 01/96286	Dec. 20, 2001	WIPO	
	WO 01/96366	Dec. 20, 2001	WIPO	
	WO 01/97794	Dec. 27, 2001	WIPO	Abstract
	WO 02/06280	Jan. 24, 2002	WIPO	

EXAMINER /Marcos Sznajdman/	DATE CONSIDERED 12/02/2010
-----------------------------	----------------------------

EXAMINER: Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with the next communication to applicant.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.S./

SUBSTITUTE FORM PTO-1449 (MODIFIED) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use several sheets if necessary) (37 C.F.R. § 1.98(b))	Attorney Docket No. 50125/102001 Serial No. 10/540,958 Applicant Stürzebecher et al. Filing Date January 3, 2006 Group 1612 IDS Filed April 8, 2010
--	--

FOREIGN PATENT OR PUBLISHED FOREIGN PATENT APPLICATION				
	WO 02/14349	Feb. 21, 2002	WIPO	
	WO 02/20475	Mar. 14, 2002	WIPO	
	WO 02/50056	Jun. 27, 2002	WIPO	
	WO 03/70229	Aug. 28, 2003	WIPO	Abstract
	WO 04/062657	Jul. 29, 2004	WIPO	

OTHER DOCUMENTS (INCLUDING AUTHOR, TITLE, DATE, PLACE OF PUBLICATION)	
	Asghar et al., "Human Plasma Kallikreins and their Inhibition by Amidino Compounds," <i>Biochim. Biophys. Acta</i> 438:250-264 (1976).
	Baker et al., "Inhibition of Cancer Cell Urokinase Plasminogen Activator by its Specific Inhibitor PAI-2 and Subsequent Effects on Extracellular matrix Degradation," <i>Cancer Research</i> 50: 4676-4684 (1990).
	Bauer, "Hilfsstoffe," in <i>Pharmazeutische Technologie</i> . Sucker et al. (eds.), Georg Thieme Verlag Stuttgart: New York, p. 174-216 (1991).
	Bookser et al., "Syntheses of Quadruply Two-and Three-Atom, Aza-Bridged, Cofacial Bis (5,10,15,20-Tetraphenylporphyrins)," <i>J. Am. Chem. Soc.</i> 113:4208-4216 (1991).
	Cajot et al., "Plasminogen-Activator Inhibitor Type 1 is a Potent Natural Inhibitor of Extracellular Matrix Degradation by Fibrosarcoma and Colon Carcinoma Cells," <i>Proc. Natl. Acad. Sci. USA</i> 87:6939-6943 (1990).
	Choi-Sledeski et al., "Discovery of an Orally Efficacious Inhibitor of Coagulation Factor Xa Which Incorporates a Neutral P _i Ligand," <i>J. Med. Chem.</i> 46:681-684 (2003).
	Collen et al., "In Vivo Studies of a Synthetic Inhibitor of Thrombin," <i>J. Lab. Clin. Med.</i> 99:76-83 (1982).
	Coussens et al., "Matrix Metalloproteinase Inhibitors and Cancer: Trials and Tribulations," <i>Science</i> 295:2387-2392 (2002).
	Dexter et al., "N,N-Dimethylformamide-induced Alteration of Cell Culture Characteristics and Loss of Tumorigenicity in Cultured Human Colon Carcinoma Cells," <i>Cancer Res.</i> 39:1020-1025 (1979).
	Dixon, "The Determination of Enzyme Inhibitor Constants," <i>Biochem. J.</i> 55:170-171 (1953).

EXAMINER /Marcos Sznaidman/	DATE CONSIDERED 12/02/2010
EXAMINER: Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with the next communication to applicant.	

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.S./

SUBSTITUTE FORM PTO-1449 U.S. DEPARTMENT OF COMMERCE (MODIFIED) PATENT AND TRADEMARK OFFICE INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use several sheets if necessary) (37 C.F.R. § 1.98(b))	Attorney Docket No. 50125/102001 Serial No. 10/540,958 Applicant Stürzebecher et al. Filing Date January 3, 2006 Group 1612 IDS Filed April 8, 2010
--	--

OTHER DOCUMENTS (INCLUDING AUTHOR, TITLE, DATE, PLACE OF PUBLICATION)	
	Duggan et al., "Urokinase Plasminogen Activator and Urokinase Plasminogen Activator Receptor in Breast Cancer," <i>Int. J. Cancer</i> 61:597-600 (1995).
	Enyedy et al., "Structure-Based Approach for the Discovery of Bis-benzamidines as Novel Inhibitors of Matriptase," <i>J. Med. Chem.</i> 44:1349-1355 (2001).
	Eriksson et al., "The Direct Thrombin Inhibitor Melagatran Followed by Oral Ximelagatran compared with Enoxaparin for the Prevention of Venous Thromboembolism after Total Hip or Knee Replacement: the EXPRESS study," <i>Journal of Thrombosis and Haemostasis</i> , 1:2490-2496 (2003).
	Fareed, et al., "Inhibition of Serine Proteases by Low Molecular Weight Peptides and Their Derivatives", <i>Ann. N. Y. Acad. Sci.</i> 370:765-784 (1981).
	Francis et al., "Comparison of Ximelagatran with Warfarin for the Prevention of Venous Thromboembolism after Total Knee Replacement," <i>N. Engl. J. Med.</i> 349:1703-1712 (2003).
	Frérot et al., "PyBOP® and PyBroP: Two reagents for the difficult coupling of the α,α -dialkyl amino acid, Aib," <i>Tetrahedron</i> , 47(2):259-270 (1991).
	Friedrich et al., "Catalytic Domain Structures of MT-SP1/Matriptase, a Matrix-degrading Transmembrane Serine Proteinase," <i>J. Biol. Chem.</i> 277:2160-2168 (2002).
	Garrett et al., "Peptide Aldehyde Inhibitors of the Kallikreins: An Investigation of Subsite Interactions with Tripeptides Containing Structural Variations at the Amino Terminus," <i>J. Pept. Res.</i> 52:60-71 (1998).
	Griffin, "Role of Surface in Surface-Dependent Activation of Hageman Factor (Blood Coagulation Factor XII)", <i>Proc. Natl. Acad. Sci. USA</i> 75:1998-2002 (1978).
	Garrett et al., "Synthesis of Potent and Selective Inhibitors of Human Plasma Kallikrein," <i>Bioorg. Med. Chem. Lett.</i> 9:301-306 (1999).
	Gustafsson et al., "Effects of Melagatran, a New Low-Molecular-Weight Thrombin Inhibitor, on Thrombin and Fibrinolytic Enzymes," <i>Thromb. Haemost.</i> 79:110-118 (1998).
	Gustafsson et al., "Effects of Inogatran, A New Low-Molecular-Weight Thrombin Inhibitor, in Rat Models of Venous and Arterial Thrombosis, Thrombolysis and Bleeding Time," <i>Blood Coagulation and Fibrinolysis</i> 7:69-79 (1996).
	Gustafsson et al., "The Direct Thrombin Inhibitor Melagatran and Its Oral Prodrug H 376/95: Intestinal Absorption Properties, Biochemical and Pharmacodynamic Effects," <i>Thromb. Res.</i> 101:171-181 (2001).
	Gustafsson et al., "A New Oral Anticoagulant: The 50-Year Challenge," <i>Nature Reviews Drug Discovery</i> 3:649-659, 2004.

EXAMINER /Marcos Sznajdman/	DATE CONSIDERED 12/02/2010
EXAMINER: Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with the next communication to applicant.	

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.S./

SUBSTITUTE FORM PTO-1449 (MODIFIED)	U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	Attorney Docket No.	50125/102001
		Serial No.	10/540,958
		Applicant	Stürzebecher et al.
		Filing Date	January 3, 2006
		Group	1612
		IDS Filed	April 8, 2010
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use several sheets if necessary)			
(37 C.F.R. § 1.98(b))			

OTHER DOCUMENTS (INCLUDING AUTHOR, TITLE, DATE, PLACE OF PUBLICATION)	
	Hara et al., "DX-9065a, a New Synthetic, Potent Anticoagulant and Selective Inhibitor for Factor Xa," <i>Thromb. Haemost.</i> 71:314-319 (1994).
	Herbert et al., "DX 9065A, a Novel, Synthetic, Selective and Orally Active Inhibitor of Factor Xa: In Vitro and In Vivo Studies," <i>J. Pharmacol. Exp. Ther.</i> 276:1030-1038 (1996).
	Ho et al., "Exploratory Solid-Phase Synthesis of Factor Xa Inhibitors: Discovery and Application of P ₃ -Heterocyclic Amides as Novel Types of Non-Basic Arginine Surrogates," <i>Bioorg. Med. Chem. Lett.</i> 9:3459-3464 (1999).
	Hooper et al., "Type II Transmembrane Serine Proteases," <i>J. Biol. Chem.</i> 276:857-860 (2001).
	Ihara et al., "Prometastatic Effect of N-Acetylglucosaminyltransferase V Is Due to Modification and Stabilization of Active Matriptase by Adding β 1-6 GlcNAc Branching," <i>J. Biol. Chem.</i> 277:16960-16967 (2002).
	Isobe, "Inhibitory Effect of Gabexate (FOY) on Contact System," <i>Blood & Vessel</i> 12:135-138 (1981).
	Judkins et al., "A Versatile Synthesis of Amidines from Nitriles Via Amidoximes," <i>Synthetic Communications</i> 26: 4351-4367 (1996).
	Kang et al., "Tissue Microarray Analysis of Hepatocyte Growth Factor/Met Pathway Components Reveals a Role for Met, Matriptase, and Hepatocyte Growth Factor Activator Inhibitor 1 in the Progression of Node-negative Breast Cancer," <i>Cancer Res.</i> 63:1101-1105 (2003).
	Kaplan, "Initiation of the Intrinsic Coagulation and Fibrinolytic Pathways of Man: The Role of Surfaces, Hageman Factor, Prekallikrein, High Molecular Weight Kininogen, and Factor XI," <i>Prog. Hemostasis Thromb.</i> 4:127-175 (1978).
	Kettner et al., "Inactivation of Trypsin-Like Enzymes with Peptides of Arginine Chloromethyl Ketone," <i>Methods in Enzymology</i> 80:826-843 (1981).
	Kettner et al., "The Selective Inhibition of Thrombin by Peptides of Boroarginine," <i>J. Biol. Chem.</i> 265, 18289-18297 (1990).
	Kettner et al., "The Selective Affinity Labeling of Factor X _a by Peptides of Arginine Chloromethyl Ketone," <i>Thromb. Res.</i> 22:645-652 (1981).
	Kim et al., "Preparation of Argatroban Analog Thrombin Inhibitors with Reduced Basic Guanidine Moiety, and Studies of Their Cell Permeability and Antithrombotic Activities," <i>Med. Chem. Res.</i> 377-383 (1996).
	Kirk, "4-Lithio-1-Tritylimidazole as a Synthetic Intermediate, Synthesis of Imidazole-4-Carboxaldehyde," <i>J. Heterocyclic Chem.</i> 22:57-59 (1985).
	Kruger et al., "Host TIMP-1 Overexpression Confers Resistance to Experimental Brain Metastasis of a Fibrosarcoma Cell Line," <i>Oncogene</i> 16:2419-2423 (1998).
EXAMINER	/Marcos Sznajdman/
	DATE CONSIDERED 12/02/2010
EXAMINER: Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with the next communication to applicant.	

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.S./

<p>SUBSTITUTE FORM PTO-1449 (MODIFIED)</p> <p>U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE</p> <p>INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use several sheets if necessary)</p> <p>(37 C.F.R. § 1.98(b))</p>	<p>Attorney Docket No. 50125/102001</p> <p>Serial No. 10/540,958</p> <p>Applicant Stürzebecher et al.</p> <p>Filing Date January 3, 2006</p> <p>Group 1612</p> <p>IDS Filed April 8, 2010</p>
---	---

OTHER DOCUMENTS (INCLUDING AUTHOR, TITLE, DATE, PLACE OF PUBLICATION)	
	Kruger et al., "The Bacterial <i>LacZ</i> Gene: An Important Tool for Metastasis Research and Evaluation of New Cancer Therapies," <i>Cancer and Metastasis Reviews</i> 17:285-294 (1999).
	Künzel et al., "4-Amidinobenzylamine-Based Inhibitors of Urokinase," <i>Bioorg. Med. Chem. Lett.</i> 12:645-648 (2002).
	Lawson et al., "Studies on the Inhibition of Human Thrombin: Effects of Plasma and Plasma Constituents Folia Haematol," <i>Leipzig</i> 109, 52-60 (1982).
	Leadley, "Coagulation Factor Xa Inhibition: Biological Background and Rationale," <i>Curr. Topics in Med. Chem.</i> , 1: 151-159 (2001).
	Lee et al., "Noncovalent Tripeptidic Thrombin Inhibitors Incorporating Amidrazone, Amine and Amidine Functions at P1," <i>Bioorg. Med. Chem. Lett.</i> 12:1017-1022 (2002).
	Lee et al., "Noncovalent Thrombin Inhibitors Incorporating an Imidazolethynyl P1," <i>Bioorganic & Medicinal Chemistry Letters</i> , 10:2775-2778 (2000).
	Lee et al., "Activation of Hepatocyte Growth Factor and Urokinase/Plasminogen Activator by Matriptase, an Epithelial Membrane Serine Protease," <i>J. Biol. Chem.</i> 275:36720-36725 (2000).
	Lin et al., "Characterization of a Novel, Membrane-bound, 80-kDa Matrix-degrading Protease from Human Breast Cancer Cells," <i>J. Biol. Chem.</i> 272:9147-9152 (1997).
	Lin et al., "Molecular Cloning of cDNA for Matriptase, a Matrix-degrading Serine Protease with Trypsin-like Activity," <i>J. Biol. Chem.</i> 274:18231-18236 (1999).
	Lin et al., "Purification and Characterization of a Complex Containing Matriptase and a Kunitz-type Serine Protease Inhibitor from Human Milk," <i>J. Biol. Chem.</i> 274:18237-18242 (1999).
	Long et al., "Synthesis and Evaluation of the Sunflower Derived Trypsin Inhibitor as a Potent Inhibitor of the Type II Transmembrane Serine Protease, Matriptase," <i>Bioorg. Med. Chem. Lett.</i> 11:2515-2519 (2001).
	Maduskuie et al., "Rational Design and Synthesis of Novel, Potent Bis-Phenylamidine Carboxylate Factor Xa Inhibitors," <i>J. Med. Chem.</i> 41:53-62 (1998).
	Maignan et al., "The Use of 3D Structural Data in the Design of Specific Factor Xa Inhibitors," <i>Curr. Topics in Med. Chem.</i> 1:161-174 (2001).
	Mignatti et al., "Biology and Biochemistry of Proteinases in Tumor Invasion," <i>Physiological Reviews</i> 73:161-195 (1993).
	Mohan et al., "Solid-Phase Synthesis of N-Substituted Amidinophenoxy Pyridines as Factor Xa Inhibitors," <i>Bioorg. Med. Chem. Lett.</i> 8:1877-1882 (1998).

EXAMINER /Marcos Sznajdman/	DATE CONSIDERED 12/02/2010
EXAMINER: Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with the next communication to applicant.	

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.S./

SUBSTITUTE FORM PTO-1449 (MODIFIED)	U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	Attorney Docket No.	50125/102001
		Serial No.	10/540,958
		Applicant	Stürzebecher et al.
		Filing Date	January 3, 2006
		Group	1612
		IDS Filed	April 8, 2010
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use several sheets if necessary)			
(37 C.F.R. § 1.98(b))			

OTHER DOCUMENTS (INCLUDING AUTHOR, TITLE, DATE, PLACE OF PUBLICATION)	
	Morrisette et al., "Low Molecular Weight Thrombin Inhibitors With Excellent Potency, Metabolic Stability, and Oral Bioavailability," <i>Bioorganic & Med. Chem. Letters</i> , 14:4161-4164 (2004).
	Muramatu et al., "Inhibitory Effects of ω -Amino Acid Esters on Trypsin, Plasmin, Plasma Kallikrein and Thrombin," <i>Biochim. Biophys. Acta</i> 242:203-208 (1971).
	Muramatu et al., "Inhibitory Effects of ω -Guanidino Acid Esters on Trypsin, Plasmin, Plasma Kallikrein and Thrombin," <i>Biochim. Biophys. Acta</i> 268:221-224 (1972).
	Muramatu et al., "Inhibitory Effects of Aryl trans-4 (Aminomethyl) Cyclohexanecarboxylate on Serine Proteases, and their Antiallergic Effects," <i>Hoppe-Seyler's Z. Physiol. Chem.</i> 363:203-211 (1982).
	Nar et al., "Structural Basis for Inhibition Promiscuity of Dual Specific Thrombin and Factor Xa Blood Coagulation Inhibitors," <i>Structure</i> , 9:29-37 (2001).
	Nelson et al., "Stereoselective Synthesis of a Potent Thrombin Inhibitor by a Novel P2-P3 Lactone Ring Opening," <i>J. Org. Chem.</i> 69:3620-3627 (2004).
	Oberst et al., "Expression of the Serine Protease Matrilysin and Its Inhibitor HAI-1 in Epithelial Ovarian Cancer: Correlation with Clinical Outcome and Tumor Clinicopathological Parameters," <i>Clin. Cancer Res.</i> 8:1101-1107 (2002).
	Ohno et al., "FOY: [Ethyl-(6-Guanidinohexanoyloxy) Benzoate] Methanesulfonate as a Serine Proteinase Inhibitor. I. Inhibition of Thrombin and Factor Xa in Vitro," <i>Thromb. Res.</i> 19:579-588 (1980).
	Okada et al., "Development of Plasmin and Plasma Kallikrein Selective Inhibitors and their Effect on M1 (Melanoma) and ht29 Cell Lines," <i>Bioorg. Med. Chem. Lett.</i> 10:2217-2221 (2000).
	Okada et al., "Development of Plasma Kallikrein Selective Inhibitors," <i>Biopolymers</i> 51:41-50 (1999).
	Okamoto et al., "Recent Studies of the Synthetic Selective Inhibitors; With Special Reference to Non-Plasmin Fibrinolytic Enzyme, Plasmin and Plasma-Kallikrein Thromb," <i>Res., Suppl. I</i> , 131-141 (1988).
	Ossowski et al., "Antibodies to Plasminogen Activator Inhibit Human Tumor Metastasis," <i>Cell</i> 35:611-619 (1983).
	Ostrem et al., "Discovery of a Novel, Potent, and Specific Family of Factor Xa Inhibitors via Combinatorial Chemistry," <i>Biochemistry</i> 37:1053-1059 (1998).
	Patani et al., "Bioisosterism: A Rational Approach in Drug Design." <i>Chem. Rev.</i> 96:3147-3176 (1996), pages 3147-3148 and 3170.
	Pauls et al., "The Design of Competitive, Small-Molecule Inhibitors of Coagulation Factor Xa," <i>Frontiers in Med. Chem.</i> , 1:129-152 (2004).

EXAMINER	/Marcos Sznajdman/	DATE CONSIDERED	12/02/2010
EXAMINER: Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with the next communication to applicant.			

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.S./

SUBSTITUTE FORM PTO-1449 U.S. DEPARTMENT OF COMMERCE (MODIFIED) PATENT AND TRADEMARK OFFICE INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use several sheets if necessary) (37 C.F.R. § 1.98(b))	Attorney Docket No.	50125/102001
	Serial No.	10/540,958
	Applicant	Stürzebecher et al.
	Filing Date	January 3, 2006
	Group	1612
	IDS Filed	April 8, 2010

OTHER DOCUMENTS (INCLUDING AUTHOR, TITLE, DATE, PLACE OF PUBLICATION)	
	Pedersen et al., "Prognostic Impact of Urokinase, Urokinase Receptor, and Type 1 Plasminogen Activator Inhibitor in Squamous and Large Cell Lung Cancer Tissue" <i>Cancer Research</i> 54:4671-4675 (1994).
	Perzborn et al., "In Vitro and In Vivo Studies of the Novel Antithrombotic Agent BAY 59-7939—an Oral, direct Factor Xa Inhibitor," <i>J. Thromb. & Haemost.</i> 3:514-521 (2005).
	Phillips et al., "Discovery of N-[2-[5-[Amino(imino)methyl]-2-hydroxyphenoxy]-3,5-difluoro-6-[3-(4,5-dihydro-1-methyl-1H-imidazol-2-yl)phenoxy]pyridin-4-yl]-N-methylglycine (ZK-807834): A Potent, Selective, and Orally Active Inhibitor of the Blood Coagulation Enzyme Factor Xa," <i>J. Med. Chem.</i> 41:3557-3562 (1998).
	Quan et al., "Bisbenzamidine Isoxazoline Derivatives as Factor Xa Inhibitors," <i>Bioorg. Med. Chem. Lett.</i> 7:2813-2818 (1997).
	Quan et al., "Discovery of 1-(3'-Aminobenzisoxazol-5'-yl)-3-trifluoromethyl-N-[2-fluoro-4-[(2'-dimethylaminomethyl)imidazol-1-yl]phenyl]-1H-pyrazole-5-carboxamide Hydrochloride (Razaxaban), a Highly Potent, Selective, and Orally Bioavailable Factor Xa Inhibitor," <i>J. Med. Chem.</i> 48:1729-1744 (2005).
	Quan et al., "The Race to Orally Active Factor Xa Inhibitor: Recent Advances," <i>Curr. Opin. In Drug Discovery & Development</i> , 7:460-469 (2004).
	Ratnoff, "Studies on the Inhibition of Ellagic Acid-Activated Hageman factor (factor XII) and Hageman factor fragments," <i>Blood</i> 57:55-58 (1981).
	Renatus et al., "Structural and Functional Analyses of Benzamidine-based Inhibitors in Complex with Trypsin: Implications for the Inhibition of Factor Xa, tPA, and Urokinase," <i>J. Med. Chem.</i> 41:5445-5456 (1998).
	Reuning et al., "Multifunctional Potential of the Plasminogen Activation System in Tumor Invasion and Metastasis (Review)," <i>International Journal of Oncology</i> 13:893-906 (1998).
	Rittle et al., "Unexpected Enhancement of Thrombin Inhibitor Potency with o-Aminoalkylbenzylamides in the P1 Position," <i>Bioorg. Med. Chem. Lett.</i> 13:3477-3482 (2003).
	Robinson et al., "Chapter 9. Anticoagulants: Inhibitors of the Factor VIIa/Tissue Factor Pathway," <i>Ann. Rep. Med. Chem.</i> 37:85-94 (2002).
	Rubini et al., "Synthesis of Isosteric Methylene-oxy Pseudopeptide Analogues as Novel Amide Bond Surrogate Units," <i>Tetrahedron</i> 43(21):6039-6045 (1986).
	Sato et al., "Antithrombotic Effects of YM-60828, a Newly Synthesized Factor Xa Inhibitor, in Rat Thrombosis Models and Its Effects on Bleeding Time," <i>Br. J. Pharmacol.</i> 123:92-96 (1998).
	Sato et al., "YM-60828, a Novel Factor Xa Inhibitor: Separation of Its Antithrombotic Effects from Its Prolongation of Bleeding Time," <i>Eur. J. Pharmacol.</i> 339:141-146 (1997).

EXAMINER	/Marcos Sznajdman/	DATE CONSIDERED	12/02/2010
EXAMINER: Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with the next communication to applicant.			

~~ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH.~~ /M.S./

SUBSTITUTE FORM PTO-1449 (MODIFIED) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use several sheets if necessary) (37 C.F.R. § 1.98(b))	Attorney Docket No.	50125/102001
	Serial No.	10/540,958
	Applicant	Stürzebecher et al.
	Filing Date	January 3, 2006
	Group	1612
	IDS Filed	April 8, 2010

OTHER DOCUMENTS (INCLUDING AUTHOR, TITLE, DATE, PLACE OF PUBLICATION)	
	Sato et al., "Medicinal Chemical Studies on Synthetic Protease Inhibitors, trans-4-Guanidinomethylcyclohexanecarboxylic Acid Aryl Esters," <i>Chem. Pharm. Bull.</i> 33:647-654 (1985).
	Schechter et al., "On the Size of the Active Site in Proteases. I. Papain," <i>Biochem. Biophys. Res. Commun.</i> 27:157-162 (1967).
	Schmitt et al., "Clinical Impact of the Plasminogen Activation System in Tumor Invasion and Metastasis: Prognostic Relevance and Target for Therapy," <i>Thrombosis and Haemostasis</i> 78:285-296 (1997).
	Shi et al., "Identification and Characterization of a Novel Matrix-degrading Protease from Hormone-dependent Human Breast Cancer Cells," <i>Cancer Res.</i> 53:1409-1415 (1993).
	Silverberg et al., "Enzymatic activities of activated and zymogen forms of human Hageman factor (factor XII)," <i>Blood</i> 60:64-70 (1982).
	Soll et al., "Amidinohydrazones as Guanidine Bioisosteres: Application to a New Class of Potent, Selective and Orally Bioavailable, Non-Amide-Based Small Molecule Thrombin Inhibitors," <i>Bioorganic & Medicinal Chemistry Letters</i> 10:1-4 (2000).
	Sperl et al., "(4-Aminomethyl) Phenylguanidine Derivates as Nonpeptidic Highly Selective Inhibitors of Human Urokinase," <i>Proc. Natl. Acad. Sci. USA</i> 97:5113-5118 (2000).
	Sperl et al., "Urethanyl-3-Amidinophenylalanine Derivatives as Inhibitors of Factor Xa. X-Ray Crystal Structure of a Trypsin/Inhibitor Complex and Modeling Studies," <i>Biol. Chem.</i> 381:321-329 (2000).
	Stauffer et al., "9-Hydroxyazafluorenes and their Use in Thrombin Inhibitors," <i>J. Med. Chem.</i> , 48: 2282-2293 (2005).
	Stephens et al., "The Urokinase Plasminogen Activator System as a Target for Prognostic Studies in Breast Cancer," <i>Breast Cancer Research and Treatment</i> , 52:99-111 (1998).
	Stürzebecher et al., "Novel Plasma Kallikrein Inhibitors of the Benzamidine Type," <i>Brazilian Journal Med. Biol. Res.</i> 27:1929-1934 (1994).
	Stürzebecher et al., "3-Amidinophenylalanine-Based Inhibitors of Urokinase," <i>Bioorganic & Medicinal Chemistry Letters</i> 9:3147-3152 (1999).
	Stürzebecher et al., "Synthesis and Structure-Activity Relationships of Potent Thrombin Inhibitors: Piperazides of 3-Amidinophenylalanine," <i>J. Med. Chem.</i> 40:3091-3099 (1997).
	Stürzebecher et al., "Synthetic Inhibitors of Bovine Factor Xa and Thrombin Comparison of Their Anticoagulant Efficiency," <i>Thromb. Res.</i> 54:245-252 (1989).
	Stürzebecher et al., <i>Zentralbl. Pharm. Pharmacother. Lab. Diagn.</i> 122:240-241 (1983).

EXAMINER	/Marcos Sznajdman/	DATE CONSIDERED	12/02/2010
EXAMINER: Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with the next communication to applicant.			

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.S./

SUBSTITUTE FORM PTO-1449 U.S. DEPARTMENT OF COMMERCE (MODIFIED) PATENT AND TRADEMARK OFFICE INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use several sheets if necessary) (37 C.F.R. § 1.98(b))	Attorney Docket No.	50125/102001
	Serial No.	10/540,958
	Applicant	Stürzebecher et al.
	Filing Date	January 3, 2006
	Group	1612
	IDS Filed	April 8, 2010

OTHER DOCUMENTS (INCLUDING AUTHOR, TITLE, DATE, PLACE OF PUBLICATION)			
	Sucker et al., <i>Pharm. Techn.</i> 2., Bauer, Georg Thieme Verlag, Stuttgart, (1991).		
	Tada et al., "Isolation of Plasma Kallikrein by High Efficiency Affinity Chromatography and Its Characterization," <i>Biol. Pharm. Bull.</i> 24:520-524 (2001).		
	Takeuchi et al., "Reverse Biochemistry: Use of Macromolecular Protease Inhibitors to Dissect Complex Biological Processes and Identify a Membrane-type Serine Protease in Epithelial Cancer and Normal Tissue," <i>Proc. Natl. Acad. Sci. USA</i> 96:11054-11061 (1999).		
	Takeuchi et al., "Cellular Localization of Membrane-type Serine Protease 1 and Identification of Protease-activated Receptor-2 and Single-chain Urokinase-type Plasminogen Activator as Substrates," <i>J. Biol. Chem.</i> 275:26333-26342 (2000).		
	Tamura et al., "Synthesis and Biological Activity of Peptidyl Aldehyde Urokinase Inhibitors," <i>Bioorganic & Medicinal Chemistry Letters</i> , 10:983-987 (2000).		
	Teno et al., "Development of Selective Inhibitors against Plasma," Kallikrein <i>Chem. Pharm. Bull.</i> 39:2930-2936 (1991).		
	Towle et al., "Inhibition of Urokinase by 4-Substituted Benzo[b]thiophene-2-Carboxamides: An Important New Class of Selective Synthetic Urokinase Inhibitor," <i>Cancer Research</i> 53:2553-2559 (1993).		
	Tucker et al., "Potent Noncovalent Thrombin Inhibitors That Utilize the Unique Amino Acid d-Dicyclohexylalanine in the P3 Position. Implications on Oral Bioavailability and Antithrombotic Efficacy," <i>J. Med. Chem.</i> 40:1565-1569 (1997).		
	Tucker et al., "Synthesis of a Series of Potent and Orally Bioavailable Thrombin Inhibitors That Utilize 3,3-Disubstituted Propionic Acid Derivatives in the P3 Position," <i>J. Med. Chem.</i> 40:3687-3693 (1997).		
	Tsuda et al., Structure-Inhibitory Activity Relationship of Plasmin and Plasma Kallikrein Inhibitors," <i>Chem. Pharm. Bull.</i> 49:1457-1463 (2001).		
	Vassalli et al., "Amiloride Selectively Inhibits the Urokinase-Type Plasminogen Activator," <i>FEB</i> 214:187-191 (1987).		
	von der Saal et al., "Derivatives of 4-Amino-Pyridine as Selective Thrombin Inhibitors," <i>Bioorganic & Medicinal Chemistry Letters</i> 7:1283-1288 (1997).		
	Wagner et al., "Synthese von N-[Aminobenzyl]-und N-[Aminophenyl]-Phthalimide und-1-Oxoisoindoline," <i>Pharmazie</i> 32:76-79 (1977).		
	Weitz, "New Anticoagulants for Treatment of Venous Thromboembolism," <i>Circulation</i> , 110:I-19-I-26 (2004).		
	Wikström et al., "Development and Validation of a Chiral Capillary Electrophoresis Method for Melagatran and Ximelagatran Drug Substances," <i>J. Sep. Sci.</i> 25:1167-1174 (2002).		
EXAMINER	/Marcos Sznajdman/	DATE CONSIDERED	12/02/2010

EXAMINER: Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with the next communication to applicant.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.S./

SUBSTITUTE FORM PTO-1449 U.S. DEPARTMENT OF COMMERCE (MODIFIED) PATENT AND TRADEMARK OFFICE INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use several sheets if necessary) (37 C.F.R. § 1.98(b))	Attorney Docket No.	50125/102001
	Serial No.	10/540,958
	Applicant	Stürzebecher et al.
	Filing Date	January 3, 2006
	Group	1612
	IDS Filed	April 8, 2010

OTHER DOCUMENTS (INCLUDING AUTHOR, TITLE, DATE, PLACE OF PUBLICATION)	
	Zeslowska et al., "Crystals of the Urokinase Type Plasminogen Activator Variant β c-uPA in Complex with Small Molecule Inhibitors Open the Way towards Structure-based Drug Design," <i>J. Mol. Biol.</i> 301:465-475 (2000).
	Zeslowska et al., "Crystals of Urokinase Type Plasminogen Activator Complexes Reveal the Binding Mode of Peptidomimetic Inhibitors," <i>J. Mol. Biol.</i> 328:109-118 (2003).
	Zhang et al., "Assignment of Human Putative Tumor Suppressor Genes ST13 (alias SNC6) and ST14 (alias SNC19) to Human Chromosome Bands 22q13 and 11q24→q25 by In Situ Hybridization," <i>Cytogenet. Cell Genet.</i> 83:56-57 (1998).
	Zhu et al., "Recent Advances in Inhibitors of Factor Xa in the Prothrombinase Complex," <i>Curr. Opin. Cardiovasc. Pulmon. Renal Invest. Drugs</i> 1:63-87 (1999).
	Office Action pertaining to U.S. Patent Application No. 10/297,557 mailed November 4, 2003.
	Office Action pertaining to U.S. Patent Application No. 10/311,364 mailed November 19, 2003.
	Office Action pertaining to U.S. Patent Application No. 10/311,364 mailed April 1, 2004.
	Office Action pertaining to U.S. Patent Application No. 10/506,579 mailed December 16, 2009.
	Office Action pertaining to U.S. Patent Application No. 10/506,579 mailed January 30, 2009.
	Office Action pertaining to U.S. Patent Application No. 10/506,579 mailed July 17, 2008.
	Office Action pertaining to U.S. Patent Application No. 10/555,821, mailed January 21, 2009.
	Office Action pertaining to U.S. Patent Application No. 10/571,026, mailed December 13, 2007
	Office Action pertaining to U.S. Patent Application No. 10/571,026, mailed February 23, 2009
	Office Action pertaining to U.S. Patent Application No. 10/571,026, mailed October 30, 2009
	International Search Report for International Application No. PCT/EP2004/000247, dated August 18, 2004
	International Preliminary Report on Patentability for International Application No. PCT/EP2004/000247, dated September 2, 2005
	Written Opinion of the International Search Authority for International Application No. PCT/EP2004/000247, dated August 18, 2004

EXAMINER	/Marcos Sznaidman/	DATE CONSIDERED	12/02/2010
EXAMINER: Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with the next communication to applicant.			

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.S./